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Jak3 expression and genomic sequence in pediatric acute lymphoblastic leukemia

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Résumé / Abstract
Janus tyrosine kinase 3 (JAK3) is one of several key regulatory enzymes in B-cell precursors which is highly conserved between multiple species. The gene for Jak3 has been mapped to human chromosome 19p12-13.1 and encompasses 23 exons. Constitutively high levels of JAK3 activity may contribute to drug resistance and enhanced clonogenicity of leukemic B-cell precursors from children and infants with acute lymphoblastic leukemia (ALL). As part of a systematic effort to accurately determine the genomic sequence of Jak3 gene in normal and leukemic B-cell precursors, we sequenced a relatively short region of Jak3 spanning two introns, originally termed introns 10 and 11. This genomic sequence appeared in certain RT-PCR products from our analysis of Jak3 gene expression in pediatric, as well as infant, primary ALL cells. Unexpectedly, a gap in the original Jak3 genomic sequence was found in intron 10 across the sequence matching to an Alu element. Furthermore, the sequence obtained from intron 11 did not match at all to that previously reported, and the length of the intron was much larger than expected at 1.1 kb. Homology to Alu elements (three regions, 699 bp total) and a LINE2 element (one region, 189 bp total) were seen across the entire region covering exons 10-12(2.1 kb total). Two potential single nucleotide polymorphisms (SNPs) were observed in intron 11. No apparent genomic mutation was found across this region in leukemic B-cell precursors from any of the ALL patients examined. This newly described sequence corrects the previous published genomic sequence from this region rather than identifying an insertion or translocation specific to these ALL cases. Our results significantly extend previous efforts to determine the genomic sequence of Jak3 and analyze its expression in childhood pro-B ALL and other forms of ALL.

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